

REMARKS

Upon entry of this amendment, Claims 1, 3-5, 14-17, 19-34, and 37-41 are pending in the present application. Among them, Claims 3, 28, and 29 are directed to non-elected species, and are withdrawn from further consideration.

Applicants note that Claims 31, 32, and 39-41 are only subject to the obviousness type double patenting rejection.

Applicants have incorporated the limitation of Claim 18 into independent Claim 1 to further clarify the subject matter claimed. As a result, Claim 18 is canceled.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

Specification Objection

The specification is objected to for containing hyperlinks and/or browser-executable codes. Applicants have amended the specification by destroying the hyperlinks and/or browser-executable codes (*e.g.*, removing “http://” or “www,” reciting “dot,” *etc.*). Reconsideration and withdrawal of the objections are respectfully requested.

Sequence Compliance

The Examiner requests Applicants to provide a sequence listing in compliance with 37 CFR 1.821(d), and to insert sequence identifiers in the claims / specification.

Applicants hereby submit a paper copy of the sequence listing together with the computer readable format (CRF), and respectfully request the Examiner to enter the sequence listing as part of the specification.

Applicants have also amended the specification and claims to insert the SEQ ID NOs.

Reconsideration and withdrawal of the specification objections are respectfully requested.

Claim Rejections under 35 U.S.C. § 102

The Office Action maintains the rejection to Claims 1, 4, 14, 19, 21-27, 30, 33, 34, and 37 under 35 U.S.C. § 102 (b) as allegedly being anticipated by Davis *et al.* (WO 00/64485, “Davis”). The Examiner argues that “fusion protein” also includes chimeric proteins generated by chemical coupling.

While Applicants disagree with this broad interpretation, Applicants have amended Claim 1 to specifically recite that the “fusion protein” is a “contranslational fusion protein encoded by a recombinant nucleic acid” (emphasis added), thereby unambiguously distinguishing the presently claimed subject matter from those disclosed in Davis. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102 (b) are respectfully requested.

Applicants wish to clarify for the record that Bhatia does not “define a fusion protein as a protein conjugate that is made either by chemical coupling or recombinant DNA technology,” as the Office Action asserts. Instead, page 571, left column, the last full paragraph of Bhatia used “chemically linked” with “conjugates,” and used “recombinant” or “express” with the anti-CEA scFv / CPG2 fusion protein. Thus Bhatia in fact supports Applicants’ position that one of skill in the art is aware of the clear distinction between chemically cross-linked conjugates and the contranslational fusion proteins presently claimed.

Claim Rejections under 35 U.S.C. § 103(a)

The Office Action maintains the rejection to Claims 1, 4, 14, 18-27, 30, 33, 34, 37, and 38 under 35 U.S.C. § 103(a) as allegedly being obvious over Davis (*supra*) in view of Bhatia *et al.* (*Intl. J. Cancer* 2000, 85, 571-577) and Whitcomb (of record).

Specifically, the Examiner states that Davis teaches a “fusion protein” wherein enzymes are chemically cross-linked to binding partners (*i.e.*, “chemically cross-linked fusion protein not a fusion protein made by cotranslation of respective genes”). The Examiner further states that protein conjugates can be made either by chemical cross-linking or by gene fusion, “but gene fusion methods have some particular advantages.” The Examiner cited the last paragraph page

571, col. 1 in Bhatia to support this argument, and argues that one of skill in the art, in view of Davis and Bhatia, would have been “motivated to make the protein conjugate of Davis *et al.* by gene fusion methodology as taught be Bhatia *et al.*”

Whitcomb allegedly teaches a mesotrypsin. The Examiner further argues that it would have been obvious to use mesotrypsin as the protease domain in a “fusion protein of Davis *et al.* by the method Bhatia *et al.*”

Applicants respectfully disagree. Applicants submit that it is improper to combine Davis with Bhatia, because doing so would require one of skill in the art to directly contradict the explicit teaching of Davis (to use chemical cross-linking) and use a method (the gene fusion method of Bhatia) that is specifically taught away by Davis.

Pursuant to MPEP 2143.01: “[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (C.C.P.A., 1959).”

Here, Davis explicitly teaches the use of chemical cross-linking for its various perceived advantages, which advantages are allegedly missing in cotranslational fusion proteins. In view of this specific teaching, one would not be *motivated* to ignore the chemical cross-linking method, and use the disfavored gene fusion methodology, despite the fact that the latter may have some other advantages not sought after in Davis. In other words, one of skill in the art would not attempt to alter the principal of operation of Davis by modifying it with the Bhatia method. There is simply cannot be a “fusion protein of Davis *et al.* by the method Bhatia *et al.*” based on the disclosure in Davis and Bhatia.

Since Whitcomb does not remedy this defect, the cited art still cannot be combined the way the Examiner suggests. Reconsideration and withdrawal of the obviousness rejection are respectfully requested.

Claims 15-17 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Davis (*supra*) in view of Bhatia *et al.* (*Supra*) and Whitcomb (of record), further in view of Guo (of record).

Guo allegedly teaches a fusion protein with a (Gly₄Ser)₃ linker. The Examiner argues that it would have been obvious for one of skill in the art to use the Guo linker in a “fusion protein as taught by David *et al.* by the method Bhatia *et al.*”

Applicants have argued above that Davis and Bhatia (and Whitcomb) cannot be combined the way the Examiner suggested, because doing so would require one of skill in the art to change the principle of operation of the prior art invention being modified. Since Guo does not remedy this defect, the cited art still cannot be combined the way the Examiner suggests. Reconsideration and withdrawal of the obviousness rejection are respectfully requested.

Double Patenting Rejection

The Office Action states that the provisional double patenting rejection will be withdrawn upon allowance when Applicants submit terminal disclaimer.

Applicants reiterate that, pursuant to MPEP 804, “[i]f the ‘provisional’ double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent [without filing a terminal disclaimer], thereby converting the ‘provisional’ double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.”

Applicants note that no claim has been issued in the co-pending application Nos. 10/792,498 and 10/650,592. Thus if the only rejection in the instant application is the provisional double patenting rejection, the Examiner should withdraw that rejection and permit the application to issue as a patent without requiring a terminal disclaimer.

If conflicting claims are first allowed in the co-pending U.S. Application No. 10/792,498 or U.S. Application No. 10/650,592, and appear in an issued U.S. patent, Applicants note that, pursuant to 37 C.F.R. § 1.130(b), a timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) may be used to overcome the double patenting rejection. Applicants will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter.

CONCLUSION

Applicants submit that the application is in condition for allowance.

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. The Director is hereby authorized to charge any other deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. **18-1945**, from which the undersigned is authorized to draw under Order No. **COTH-P02-001**.

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Respectfully submitted,

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